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PATENT & TRADEMARK OFFICE

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Docket No.: C15043/174944

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of :	)	
Harold M. Bates	)	Examiner: D. Venci
Serial No.: 10/777,543	)	Art Unit: 1641
Filed: February 12, 2004	)	
For: DETECTION OF ASYMPTOMATIC CORONARY ARTERY DISEASE USING ATHEROGENIC PROTEINS AND ACUTE PHASE REACTANTS	)	

RESPONSE TO OCTOBER 10, 2006 OFFICE ACTION

Mail Stop Amendment
Commissioner For Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In response to the October 10, 2006 Office Action, in which the Examiner required restriction between two groups of claims and election of species, applicant, with traverse, hereby elects:

- the Group I claims (claims 1-9, 11-13, 15-30, 32-34, and 36-42),
- OxLDL as the atherogenic protein,
- C-reactive protein as the acute phase reactant, and
- stable angina as the coronary artery disease stage (provided, however, that applicant would prefer to and hereby conditionally elects "asymptomatic coronary artery disease," which was not listed by the Examiner as a choice but which should have been listed).

Applicant hopes the Examiner will reconsider the requirements he made in the Office Action because they seem to be premised on a misunderstanding of the invention and the clams.

The Group I claims are not "drawn to methods comprising 'asymptomatic patients'" nor are the Group II claims (nos. 43-88) "drawn to methods comprising patients staged for coronary artery disease."

Furthermore, there is no reason to classify the two groups of claims in different classes, and the classes/subclasses identified by the Examiner for the two groups of claims are puzzling. The Examiner said the Group I claims could be classified, for example, in 434/156 and the Group II claims, for example, in 436/815. However, according to the USPTO website, 434/156 is "Education And Demonstration/Language" and 436/815 is "Chemistry: Analytical And Immunological Testing/Test For Named Compound Or Class Of Compounds." The former is clearly way off the mark for the Group I claims and the latter is only somewhat closer to the Group II claims.[1] The Examiner did not give any good reason for saying the two groups of claims could be classified in different classes and he did not properly identify those different classes.

Finally, applicant does not understand why the Examiner said Invention I (the Group I claims) "requires a contradiction" and why the Group I claims are "indefinite."

As set forth in the application, the invention relates to the field of coronary artery disease ("CAD"). An individual either does not have the disease ("no disease") or has the disease (is in a "diseased state"). The diseased states may be subdivided into (a) asymptomatic (i.e., without symptoms or symptomless) disease, and (b) symptomatic (i.e., with symptoms) disease. Another way of dividing up the continuum of the diseased states is (1) non-acute, which includes asymptomatic CAD and stable angina, and (2) acute, which includes unstable angina and acute myocardial infarction (heart attack). See application, e.g., page 10, lines 23-25. This may be illustrated as follows.

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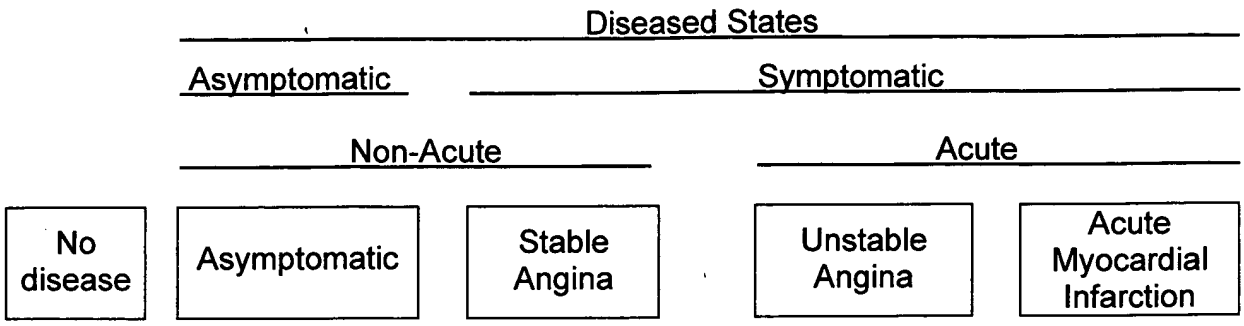
[1] Even assuming the former (434/156) was supposed to be 4<u>2</u>4/156, there is no such subclass and 424/156.1 (the closest subclass to 424/156) is sub-indented under 424/155.1, which concerns cancer and would seem to be irrelevant to coronary artery disease. If the "434/156" was supposed to be 43<u>6</u>/156, that would be "Chemistry: Analytical And Immunological Testing/Pyrolysis, Combustion, Or Elevated Temperature Conversion – Explosibility," which is also irrelevant.



As shown above, there are five states, one in which there is no disease (first box at left) and four in which there is disease: Asymptomatic disease (second box from the left), Stable Angina (third box from the left), Unstable Angina (fourth box from the left), and Acute Myocardial Infarction (fifth box from the left). Of the four diseased states shown, Asymptomatic CAD (second box from the left) is the mildest and Acute Myocardial Infarction is the most serious.

Asymptomatic disease (second box from the left) is asymptomatic and non-acute, Stable Angina (third box from the left) is symptomatic and non-acute, Unstable Angina (fourth box from the left) is symptomatic and acute, and Acute Myocardial Infarction (fifth box from the left) is symptomatic and acute. Someone with asymptomatic CAD does not display any symptoms, e.g., does not have chest pains caused by insufficient blood flow to the coronary artery, but he or she ***does*** have the disease.

A person having CAD and not changing his or her lifestyle and/or taking medication to halt the disease and who lives long enough will almost certainly progress from asymptomatic to stable angina to unstable angina to acute myocardial infarction (some individuals may appear to proceed directly from asymptomatic CAD to acute myocardial infarction because their angina presents so briefly).

U. S. Patent No. 6,309,888 describes one approach for determining where an individual should likely be placed on the entire no-disease/disease continuum (see application, page 10, line 20 et seq.).

The present invention employs another approach, namely, using an atherogenic protein (e.g., OxLDL), an acute phase reactant (e.g., C-reactive protein), and optionally an anti-atherogenic protein (e.g., HDL). After the individual's values for an atherogenic

protein, an acute phase reactant, and optionally an anti-atherogenic protein have been obtained, the two values (or three values if the anti-atherogenic protein is also used) are used to determine where on the continuum the individual should likely be placed, in other words, to assess the likelihood that the individual has a stage of the disease.

As shown in the application, higher values of the "bad" substances (atherogenic protein and positive acute phase reactant) tend to indicate a more serious CAD state and higher values of the "good" substance (anti-atherogenic protein) tend to indicate a less serious CAD state. Depending on which substances are utilized and what stage of the disease is of interest to the clinician, one or more cut-points are readily established and then the assessment can be made depending on the comparison made to the one or more cut-points.

Table III of the application shows analytical values for various sub-populations and Table IV shows how those values may be manipulated together to determine a single characterizing value, which can then be compared to a single appropriate cut-point. Thus, in the first data line of Table IV, OxLDL (atherogenic protein) multiplied by C-reactive protein (acute phase reactant) yields a value of 2.87 for the control (no disease) group, a value of 16.6 for the stable angina group, and a value of 55.0 for the combined acute group of those with unstable angina and acute myocardial infarction.[2]

As explained in the application, there are a number of ways of using the two (or optionally three) values for a patient, each different way requiring a different one or more cut-points (see, application, page 23, line 29, through page 25, Table I). The first data line of Table IV uses an atherogenic protein and an acute phase reactant together, which is within the second choice (i.e., the column labeled "(ii)") of Table I. As shown in Table I, the combination of the atherogenic protein and acute phase reactant is compared to a single cut-point.

If one were interested in determining which of the diseased states individuals with and without symptoms likely had, cut-points could be established for each of the stages of interest and the values for the individuals could be compared to each of the cut-points to make the assessment. If one were interested in making a more particular

[2] The values in Table IV and the advantages of the invention are discussed at length following Table IV, starting on application page 44 through the top of page 47.

assessment, namely, to assess whether individuals without symptoms had asymptomatic CAD, establishing cut-points for all of the diseased states would not be necessary because if the individuals had any symptoms, by definition they would not be asymptomatic. Thus, for the symptomless individuals of interest, if their atherogenic protein and acute phase reactant values (with or without the optional anti-atherogenic protein values) were high enough, the assessment could be made that they were likely to have asymptomatic CAD (see, e.g., application, page 47, lines 3-20).

Turning now to the claims, there are two independent claims in Group I, namely, claims 1 and 22, and there are two independent claims in Group II, namely, claims 43 and 66. The beginning of each of the four independent claims is as follows:

> Group I
>
> 1. A method of making an assessment of the likelihood that a human patient who is asymptomatic for coronary artery disease has the disease, the method comprising the steps: ....
>
> 22. A method of facilitating the assessment by a medical professional of the likelihood that a human patient who is asymptomatic for coronary artery disease has the disease, the method comprising the steps: ....
>
> Group II
>
> 43. A method of making an assessment of the likelihood that a human patient has a stage of coronary artery disease, the method comprising the steps: ....
>
> 66. A method of facilitating the assessment by a medical professional of the likelihood that a human patient has a stage of coronary artery disease, the method comprising the steps: ....

Accordingly, applicant does not understand the Examiner's assertion that the Group I claims are drawn to methods "comprising 'asymptomatic patient.'" The methods of claims 1 and 22 comprise steps, *not patients*, and the steps include obtaining levels of substances in samples from the patients, obtaining one or more cut-points, etc. so that an assessment can be made of the likelihood **that a patient who is asymptomatic for coronary artery disease has the disease.**

The Examiner also stated that the Group II claims are "drawn to methods comprising patients staged for coronary artery disease." However, the methods of claims 43 and 66 comprise steps, *not patients*, and the steps include obtaining levels of substances in samples from the patients, obtaining one or more cut-points, etc. so that an assessment can be made of the likelihood **that a patient has a stage of coronary artery disease**.

As explained above, **one the stages of coronary artery disease is asymptomatic CAD**. Thus, contrary to the Examiner's assertion that the two groups of claims are "unrelated," it is clear that they certainly are related and in fact are "related processes" as that term is used in MPEP § 806.05(j) (Revision 5, August 2006). If the Examiner will compare claim 1 (in Group I) to claim 43 (in Group II) and claim 22 (in Group I) to claim 66 (in Group II), he will see just how related the two groups of claims are.

The Examiner says they are unrelated because they have "different modes of operation" because the Group I claims require a "contradiction" while the Group II claims require patients staged for coronary artery disease. The Examiner goes on to assert that the Group I claims are "indefinite," presumably because of the supposed "contradiction."

Applicant is unaware of any "contradiction" in the Group I claims and would appreciate the Examiner's explaining in detail what he means (the alleged "contradiction" was not even identified in the Office Action). Furthermore, **fundamental fairness would seem to require that applicant be allowed to respond to that explanation *if the restriction requirement is going to be made final***.

The Examiner also asserts that the scopes of prior art searches for the two groups of claims are not co-extensive, apparently based on his belief that the Group I

claims are "indefinite," which presumably is based on the his belief that they "require[] a contradiction." Assuming the Examiner identifies the alleged "contradiction" and allows applicant to explain why there is no "contradiction," the restriction requirement should be withdrawn.

MPEP § 806.05(j) instructs that Examiner that:

> [t]o support a requirement for restriction between two or more related product inventions, or between two or more related process inventions, both two-way distinctness and reasons for insisting on restriction are necessary, i.e., separate classification, status in the art, or field of search. [Emphasis added]

The two groups of claims ***are*** for "related processes," the two groups ***should be*** classified the same, they ***do have*** the same "status in the art," and their fields of search ***are*** co-extensive. The Examiner cannot show two-way distinctness, nor can he show sound reasons for insisting on restriction.

At to the election of species, applicant has elected "OxLDL" as the atherogenic protein, "C-reactive protein" as the acute phase reactant, and "stable angina" as the stage of coronary artery disease.

As should be clear from the preceding discussion, there is another stage of the disease that should have been listed and thereby given to applicant as a choice: asymptomatic coronary artery disease. Applicant would have elected "asymptomatic coronary artery disease" if it had been listed by the Examiner. Assuming the Examiner reconsiders and makes it a choice, applicant hereby elects "asymptomatic coronary artery disease" instead of "stable angina," the choice applicant was forced to make because "asymptomatic coronary artery disease" was not listed.[3]

[3] The election of "asymptomatic coronary artery disease" would again highlight the fact that the two sets of claims concern "related processes" as that term is used in MPEP § 806.05(j).

* * *

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Favorable consideration of all claims and allowance are respectfully requested.

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to Mail Stop Amendment, Commissioner For Patents, P.O. Box 1450, Alexandria, VA 22313-1450

on November 6, 2006
(Date of Deposit)

Stephen P. Gilbert
Signature

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